Pharmacy and Therapeutics Committee Meeting Record

Date: January 16, 2009 **Time:** 9:00 a.m. – 3:30 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Conference Room D

Moderator: Phil Petersen, M.D.

Committee Members Present: Phil Petersen, M.D.-Chair; Stan Eisele, M.D.; Perry Brown, M.D.; William Woodhouse, M.D.; Catherine Hitt PharmD; Tim Rambur, PharmD; Mark Johnston, RPh; Dennis Tofteland, RPh;

Others Present: Steve Liles, PharmD; Selma Gearhardt, PharmD; Bob Faller; Rachel Strutton

Committee Members Absent: Michelle Miles, PA-C; Tami Eide, PharmD

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	Dr. Petersen	Dr. Petersen called the meeting to order.
Committee Business		
➢ *Roll Call*	Phil Petersen, M.D.	Dr. Petersen completed the Roll Call and welcomed the P&T Committee members.
➢ *Introduction of new Committee member*	Phil Petersen, M.D.	Dr. Petersen introduced Dr. Perry Brown and welcomed him to the P&T Committee. Dr. Brown's term began January 1, 2009.
➢ *Reading of Confidentiality Statement*	Phil Petersen, M.D.	Dr. Petersen read the Confidentiality Statement.
➢ *Approval of Minutes from August 15, 2008 Meeting*	Phil Petersen, M.D.	There were no corrections. Minutes were accepted as proposed.
➢ *Updated Department Guidelines for the Operation of the Idaho Medicaid P&T Committee*	Phil Petersen, M.D.	Dr. Petersen brought to the attention of the P&T Committee an updated document "*Department Guidelines for the Operation of the Medicaid P&T Committee"* that had been provided to the P&T Committee members in their meeting packets. The updated guidelines were mentioned as material to be taken and reviewed by the Committee members after the meeting. The Committee members were asked to contact the Division of Medicaid's Pharmacy Unit with any suggested changes.

Public Comment Period	Phil Petersen, M.D. Bob Faller, Medical Program Specialist	Twenty one (21) people signed up to speak during the public comment period. Public testimony was received from the following speakers:

Speaker	Representing	Agent	Class
Alex Mori	Forest Laboratories	Bystolic	Beta Blockers
Nick Allen, PAC	Idaho Urology Institute	Detrol LA	Bladder Relaxant Preparations
Dr. Donald Hartman	Forest Laboratories	Bystolic	Beta Blockers
Dr. Arnold Silva	Forest Laboratories	Bystolic	Beta Blockers
Dr. Arnold Silva	Novartis	Tekturna	Angiotensin Modulators
Dr. Ed Newcombe	Pfizer	Lipitor	Lipotropics, Statins
Dr. Will Watkins	GlaxoSmithKline	Avodart	BPH Treatment
Mandy Hosford	AstraZeneca	Crestor	Lipotropics, Statins
Mandy Hosford	AstraZeneca	Nexium	Proton Pump Inhibitors
Dr. Roy Palmer	Pfizer	Lipitor	Lipotropics, Statins
Jennifer Brzana	GlaxoSmithKline	Avodart	BPH Treatment
David Nilson	GlaxoSmithKline	Arixtra	Anticoagulants, Injectable
Pam Sardo	Abbott Laboratories	Tricor	Lipotropics, Other
Pam Sardo	Abbott Laboratories	Simcor	Lipotropics, Statins
Aaron Huwe	Gilead Sciences	Letairis	PAH Agents, Oral
Dr. An Phan	Schering	Zetia/Vytorin	Lipotropics, Other
Leigh Platte	Astellas	Vesicare	Bladder Relaxant Preparations
Jon Beaty	Boehinger Ingelheim	Micardis	Angiotensin Modulators
Jon Beaty	Boehinger Ingelheim	Flomax	BPH Treatment
Long Nguyeu	GlaxoSmithKline	Lovaza	Lipotropics, Other
Dina Noble	Allergan	Sanctura XR	Bladder Relaxant Preparations
Sue Heineman	Pfizer	Detrol LA	Bladder Relaxant Preparations

Drug Class Reviews and Committee Recommendations		Drug Class Reviews and Committee Recommendations
➢ Hypoglycemics, TZD	Susan Carson, MPH OHSU EPC	<u>Hypoglycemics, TZD</u> Ms. Carson reviewed the results of a September 2008, update to the drug class review on Thiazolidinediones (TZDs). This report updated an AHRQ report published in 2006. The updated report addressed both within-and between-class comparisons of rosiglitazone and pioglitazone and other diabetes treatments, with particular focus on efficacy, effectiveness and adverse events (AE). The update concluded that TZDs have similar efficacy for reducing A1C between TZDs & other oral hypoglycemic agents, and that rosiglitazone shows an increase risk of heart failure vs. other agents. Rosiglitazone prevented incidence of diabetes in a person with pre-diabetes or metabolic syndrome, but increased the risk of heart failure. Adverse effects were similar for the both TZD's. However there was more heart failure and edema but less risk of hypoglycemic episodes with the TZD's verses other hypoglycemic agents. **Committee Recommendations** The Committee felt there was no evidence to recommend changes to this drug class.
➢ Hypoglycemics, Meglitinides	Steve Liles, PharmD	<u>Hypoglycemics, Meglitinides</u> This drug class was last reviewed January 2008. Dr. Liles noted that the ADA Consensus Algorithm (2008), management of Type 2 diabetes does not include meglitinides. He also noted a new combination of Prandin & metformin, PrandiMet. **Committee Recommendations** The Committee felt there were no reasons to include or not include any of the agents on the PDL. Utilization of this drug class in the State of Idaho is not significant. There does not seem to be consequential differences in efficacy and safety, so the Committee recommended no change to the existing PDL.

➢ Beta Blockers	Steve Liles, PharmD	<u>Beta Blockers</u> This drug class was last reviewed October 2007. Dr. Liles provided an overview of a new drug in this class Bystolic (nebivolol). Two (2) new clinical trials were reviewed regarding nebivolol vs. atenolol. He also mentioned that Toprol XL is now available generically. **Committee Recommendations** The Committee recommended that all preferred agents remain on the PDL. The Committee stated that either carvedilol or metroprolol be required on the PDL for heart failure. The consensus was that the new agent Bystolic did not need to be available as a first line agent.
➢ Calcium Channel Blockers	Steve Liles, PharmD	<u>Calcium Channel Blockers</u> This drug class was last reviewed October 2007. Dr. Liles presented the current PDL and mentioned that Sular was now available as a new formulation with different strengths, while the previous formulation of Sular is available generically. The Committee reviewed the updated guidelines from the ADA on standards of treatment for diabetic patients and two (2) new clinical trials regarding patients with hypertension and heart failure. Per the guidelines, Dyhydropyridine Calcium Channel Blockers are second line therapy. **Committee Recommendations** The Committee stated that either diltiazem or verapamil must be prefered. The Committee recommended that the long acting products isradipine and nicardipine remain non-preferred. The Committee felt there was no clinical reason to include or exclude nisoldipine. They asked Idaho Medicaid to look at cost data for the new formulation of Sular and the new generic nisoldipine.
➢ Angiotensin Modulators	Steve Liles, PharmD	<u>Angiotensin Modulators</u> This drug class was last reviewed January 2008. This drug class includes ACE Inhibitors, ACE Inhibitors/hydrochlorothiazide combinations, Angiotensin Receptor Blockers (ARBs), ARBs/HCTZ combinations and the Direct Renin Inhibitor, Tekturna®. Dr. Liles noted that Tekturna is now available in combination with HCTZ, generic ramipril is now available and that valsartan is now indicated for HTN in children down to the age of six (6). He provided six (6) new clinical trials and three (3) Meta-Analyses. **Committee Recommendations** The Committee recommended Tekturna® be a second line agent, and ACE Inhibitors be included on the PDL. They concluded that the ARBs have no new clinical evidence to change their PDL status. The Committee recommended that women of child bearing age receive safety warnings through the DUR, PDL or PA form.

Drug Class Reviews and Committee Recommendations (cont.)		Drug Class Reviews and Committee Recommendations (cont.)
➢ Angiotensin II Receptor Blockers	Steve Liles, PharmD	<u>Angiotensin II Receptor Blockers</u> Information for this drug class was included in the Angiotensin Modulators information noted above.
➢ Angiotensin Modulators/CCB Combo Drugs	Steve Liles, PharmD	<u>Angiotensin Modulators/CCB Combo Drugs</u> This drug class was last reviewed January 2008. Dr. Liles shared one (1) discontinued product Lexxel – felodipine ER/enalapril with the Committee, as well as a new indication for Exforge as a first line therapy in patients requiring multiple medications. The Committee reviewed two (2) new clinical trials. Concerns about flexibility in dosing, with fixed dosed combinations, were discussed. **Committee Recommendations** The Committee recommended no changes to the PDL for this drug class.
➢ Lipotropics, Statins	Steve Liles, PharmD	<u>Lipotropics, Statins</u> This drug class was last reviewed January 2008. Dr. Liles provided an overview of one (1) new combination product Simcor, a combination of simvastatin and niacin ER , which is indicated when simvastatin monotherapy is not adequate. Simcor was shown superior to simvastatin alone in clinical trials. The Committee reviewed three (3) new clinical trials and two (2) Meta-Analyses. **Committee Recommendations** The Committee felt there was evidence based differences in potency amongst the statins. The Committee felt it important to have one high potency drug (Crestor or Lipitor) as a preferred agent. The Committee recommended maintaining the current drug class structure on the PDL, with one (1) of the high potency drugs as a preferred agent.

➢ Lipoptropics, Other	Steve Liles, PharmD	Lipoptropics, Other This drug class was last reviewed January 2008. Dr. Liles provided an overview of two (2) new dosage forms of fenofibrate, Lipofen (fenofibrate 150mg) and Fenoglide (fenofibrate 120mg) as well as a new indication for colesevelam for glycemic control in adults with type 2 diabetes. The Committee reviewed two (2) new clinical trials. **Committee Recommendations** The Committee recommended PDL decisions regarding the Fibric Acid derivatives be cost based, but no change in PDL status for all other products. The Committee recommended therapeutic PA, for Lovaza due to hypertriglyceriderma.
➢ Anticoagulants, Injectable	Steve Liles, PharmD	Anticoagulants, Injectable This drug class was last reviewed October 2007. There was no new clinical data to share with the Committee. **Committee Recommendations** The Committee has no recommendations for change in this drug class.
➢ Cough and Cold Products	Steve Liles, PharmD	Cough and Cold Products This is Idaho Medicaid's first review of this drug class. This drug class encompasses non-cough suppressant, narcotic cough suppressant and non-narcotic cough suppressant formulations. Dr. Liles provided the AACP guidelines for this class. Dr. Liles also presented the current warnings from the CDC and FDA, drug-drug interactions and potential adverse effects. The Committee reviewed one (1) Meta-Analysis. **Committee Recommendations** Per the FDA 2007 Pediatric Advisory Committee warning, the P&T Committee recommended restricting use of cough and cold products for participants six years of age and younger. They recommended that OTC agents be authorized for use when cost effective. A four (4) ounce quantity restriction and a two (2) fill limit per participant, every six (6) months was recommended.
➢ PAH Agents, Oral	Steve Liles, PharmD	PAH Agents, Oral This is Idaho Medicaid's first review of this drug class. Dr. Liles discussed the three medications in this new drug class, Letairis (ambrisentan), Tracleer (bosentan) and Revatio (sildenafil), their indications, adverse effects profile and dosage regimens. The Committee reviewed the 2007 ACCP guidelines and warnings, as well as four (4) clinical trials.

		Committee Recommendations The Committee recommended listing all agents in this drug class as preferred without restrictions but to monitor the use of Revatio.
➢ Bladder Relaxant Preparations	Steve Liles, PharmD	<u>Bladder Relaxant Preparations</u> This drug class was last reviewed October 2007. There was no new clinical data to share with the Committee. **Committee Recommendations** The Committee recommended no changes to the PDL for this drug class.
➢ BPH Agents	Steve Liles, PharmD	<u>BPH Agents</u> This drug class was last reviewed October 2007. Dr. Liles provided a recent study that detailed the use of Avodart (dutasteride) in combination with Flomax (tamsulosin). The combination was more effective than monotherapy. **Committee Recommendations** The Committee recommended no changes to the PDL for this drug class. However, if there were financial reasons for change, the Committee recommends that either Flomax or Uroxatral remain as a preferred agent.
➢ Erythropoiesis Stimulating Proteins	Steve Liles, PharmD	<u>Erythropoiesis Stimulating Proteins</u> This drug class was last reviewed January 2008. The Committee reviewed one (1) Meta-Analysis regarding patients with anemia and cancer. **Committee Recommendations** The Committee recommended no changes to the PDL for this drug class.
➢ Phosphate Binders	Steve Liles, PharmD	<u>Phosphate Binders</u> This drug class was last reviewed October 2007. Dr. Liles provided an overview of one (1) new product Renvela (sevelamer carbonate), which may have a lower incidence of overall GI events. Renvela is replacing Renagel (sevelamer HCl) in the market place and Genzyme wants to transition all patients on Renagel to Renvela by September of 2009. **Committee Recommendations** The Committee recommended no changes to the PDL for this drug class.

➢ Proton Pump Inhibitors	Steve Liles, PharmD	<u>Proton Pump Inhibitors</u> This drug class was last reviewed January 2008. Dr. Liles provided an overview of the product changes, Protonix (pantoprazole) is now available as a new generic and Prevacid Suspension is off the market. Aciphex (rabeprazole) has a new indication for short term treatment of GERD in patients as young as 12 years old, and Nexium (esomeprazole) for healing erosive esophagitis in patients as young as one year old. **Committee Recommendations** The Committee recommended no changes to the PDL for this drug class, but to remain cost effective.

Pharmacy and Therapeutics Committee
Public Comment
January 16, 2009

Alex Mori

Good morning ladies and gentlemen of the Committee. My name is Alex Mori and I'm a scientist and therapeutic specialist for Forest Laboratories. I'm here today to provide you information regarding Bystolic, a drug also known by the name nebivolol, a new beta blocker approved by the FDA in December 2007, for the treatment of hypertension. For over forty years, suppression of beta-adrenergic signaling through the use of beta blockers has been shown to improve all-cause mortality and cerebrovascular outcomes. This has led to [illegible] to recommend that along with other drugs, beta blockers should be used as both first-line and add-on therapy for the treatment of hypertension. Significant heterogeneity, however, exists within the beta blocker class of drugs, including on their cardioselectivity, as well as in their abilities to vasodilate. Nebivolol shows the highest beta-1 selectivity of any beta blocker currently available in the United States. Moreover, nebivolol is vasodilatory. This effect, unlike other vasodilatory beta blockers is not caused by action on alpha adrenergic signaling, but rather through enhancement of nitric oxide bioavailability in the vascular endothelium. Nebivolol is currently the only beta blocker to be both cardioselective and vasodilatory. Worldwide, over 70 clinical trials involving nebivolol have been completed, including comparative trials with beta blockers, ACE inhibitors, angiotensin receptor blockers, and calcium channel blockers. These trials have established nebivolol's effectiveness as an antihypertensive agent in a broad range of patients. Within the United States, as part of the FDA's new drug application process, three studies were included in over 2,000 patients. Two of these studies were recently published in the Journal of Clinical Hypertension in 2007. In pooled analysis of these trials, nebivolol demonstrated significant dose related decreases in both diastolic and systolic blood pressure. The blood pressure lowering effect was evident within the first two weeks' of treatment and was maintained over the 24-hour dosing period. Furthermore, because beta blockers are traditionally less effective in reducing blood pressure in African Americans, one of these studies was exclusively done in African Americans, where it was basically shown to reduce blood pressure to a similar extent as in the total cohort. Traditionally, beta blockers lower blood pressure primarily by reducing cardiac output. They also increase peripheral vascular resistance, leading to notorious side effects associated with traditional beta blockers including fatigue, cold extremities and sexual dysfunction. By contrast, because of nebivolol's vasodilatory properties, it preserves cardiac output while reducing peripheral vascular resistance. This hemodynamic profile largely eliminates negative side effects and metabolic effects experienced with traditional beta blockers. In a study published in the American Journal of Cardiology in 2003, a two-week treatment with nebivolol 5 mg daily versus atenolol 100 mg daily demonstrated similar blood pressure reductions. However, whereas atenolol reduced cardiac output by more than 20% within this period of time and increased peripheral vascular resistance, nebivolol maintained cardiac output while reducing peripheral vascular resistance. The authors of this study then conclude that the reduction in peripheral vascular resistance along with increased stroke volume allows for a decrease in blood pressure with a preservation of cardiac output. In another longer term, open label study undertaken by Cleophas et al, 3,741 patients, all of whom were hypertensive, both treated and untreated, received 5 mg of nebivolol daily for six months. This study which is reflective of conditions encountered in real world clinical practice, showed statistically significant reductions in blood pressure at six months compared to that at two weeks. Moreover, while on nebivolol, incidence of cold

extremities, sexual dysfunction and fatigue occurred at rates no higher than those previously reported for these patients when they were on ACE inhibitors, ARBs or calcium channel blockers.

Nicholas Allen, PA-C

Nick's fine. I go by Nick and I'm a physician assistant and I work with Idaho Urologic Institute. I'm not representing a drug company. I'm speaking on behalf of Detrol LA. We just finished a review; we have a larger urologic group and we get a chance to look at several drugs and what is prescribed in our practice. Detrol LA is the second most prescribed OAB medication that we use. It's very effective and you guys are considering taking it off the formulary. We found something interesting that I just wanted to bring up and make you aware of. About 20% of our patients fail OAB medications of any class that we use. Of those 20%, they go on to further imaging, testing, cystoscopy and CMG/EMG studies, which the cost of just one of those studies pays for any one of the drugs you have on formulary if you bought that drug at $60 per month for about 2.5 years. By eliminating any drug, I don't care which one it is, really, that you take off the formulary, you're going to increase the number of studies that we do, therefore increasing the cost of health care provided for overactive bladder and incontinence. Detrol LA is the second drug that we use. It's in our procedure formula for our Idaho Urologic Institute as one of the first-line choices with our clinical patients. If they've been on it already and they come to us, we obviously don't use it first-line, but by removing one of those, we believe as a group, and this represents all of us at the Idaho Urologic Institute, specifically involved in the review are Dr. King, Dr. Fairfax, Dr. Waltman, myself, and the other physician's assistant, Derek Durkus, we think you'll in turn increase the cost of health care for this specific entity over a period of a couple of years. Again, like I said, the bottom line is cost of procedural intervention. It's not our practice to start with procedural intervention; you fail three OAB drugs before CMG or cystoscopy is ordered, unless there's an underlying illness, like rectocele, cystocele or prostatic surgery in males. So, that's the take-home message. Thank you for your time.

Donald Hartman, MD

Hello, my name is Donald David Hartman, MD, and I'm a board certified lipidologist and also board certified in Family Practice. I do see Medicaid patients and I am commenting on nebivolol (Bystolic). I am a speaker on Forest speaker's guild. We as lipidologist feel that the only beta blockers that should be used are carvedilol and nebivolol. Speaking for our group of four board certified lipidologists, nebivolol's currently indicated in this country for hypertension, but in Europe, there are multiple indications; congestive heart failure post MI, and lots of studies with that. I don't feel that metoprolol or atenolol should be used at all, except in extremely rare cases. The reason being is that they increase insulin resistance. Insulin resistance is thought by most hypertensive experts as being the cause of 95% of essential hypertension. With drugs like thiazide diuretics, metoprolol and atenolol, you'll actually see the HDL go down, the triglycerides go up, and uric acid go up, so you're actually worsening the underlying condition. When I see patients come in to me for consultations and they're on metoprolol or atenolol, that's a fairly easy one, because I can switch them to either nebivolol or carvedilol and get their HDL to come up, their triglycerides to come down, their HA1cs to come down, we see their insulin levels come down, and glucose levels come down. We've used nebivolol quite a bit over the last year. It's neutral with lipids and insulin resistance and very well tolerated, and I prefer it over carvedilol because carvedilol is twice a day and as you know, compliance is not as good and you seem to see a little bit more dizziness with the carvedilol. I'm also a taxpayer and if Forest were to give a very good price on this drug, I think it would be a fine addition to the formulary. I think for hypertension it's definitely superior to generic carvedilol being b.i.d. and Coreg CR is much more expensive as far as the price. In the area, it's about 2.5-3 times as expensive as Bystolic. We don't use it first line in hypertension, except rarely, but as far as an add-on, we consider ACE inhibitors, ARBs, to be first-line in nearly all hypertension, but

as you know with diabetic patients and severe hypertensives, many of them require two or three agents or more. If you look back at UK PDS, diabetic patients to get their blood pressure to control, I think it was up there, 3-5 agents or even more sometimes. Now if we use agents that actually decrease insulin resistance, Actos (pioglitazone), and don't use any agents which increase insulin resistance, it's much easier to get the blood pressure under control and, thus, delay end organ damage. Thank you.

Committee: How many people do you see where you are initiating therapy? I mean, is that very common for you, or do you typically see the patient when therapy has already been initiated?
Answer: Well, I mean, I do primary care as well as lipidology, so I see lots of so-called virgin hypertensives, diabetics, and they supply lots of these samples, so it's easy to get them going even for several months before, you know, having to pay for it. But yeah, we get consults in, but then a lot of patients are primary care patients. We do primary care as well as lipidology.
Committee: And what percentage of your practice is Medicaid?
Answer: Probably less than 5%. Thank you.

Arnold Silva, MD
Good morning, I'm Arnold Silva. I'm a nephrologist with Boise Kidney & Hypertension. I've actually been asked to speak on two different classes of agents, so I guess I'll just continue first with Bystolic, since we've been talking about nebivolol. We've heard a lot about this drug. I'll try to add a little bit of my perspective as a nephrologist. By the time people come to me, they're already on two, three, and sometimes even more drugs, so I'm often looking for an additional agent that when added to their existing regimen of antihypertensives, will not only be effective, but also well tolerated, and in thinking about therapies, the beta blocker class, at least for me, has not been something that I've traditionally used and Bystolic has changed a lot of that, in part because of its tolerability, and when you look at quality of life studies, a lot of this data comes out of Europe, this drug is very well tolerated and compares really to the angiotensin receptor blocker class as far as overall quality of life when you look at three- and six-month data, and that's been looked at versus Cozaar which is the ARB that we've had the longest. So I think tolerability is an important issue. It's a good, once-a-day drug and, given all the antihypertensives that my patients are on, I try to do a once-a-day drug with everything, and the 24-hour ambulatory blood pressure data certainly supports this as a once-a-day drug, and I will echo the sentiments of Dr. Hartman in saying that I think the metabolic issues of hypertension are also quite important, so we want a beta blocker that's going to be metabolically neutral, which this drug is at the very least metabolically neutral, along with the trend of improving insulin sensitivity. So I think for several reasons, it makes a very good drug as far as the overall regimen of hypertension is concerned. People will say "Well, you've got so many classes of drugs and do you need a beta blocker in your therapeutic regimen?". I think for many patients, you do, because most patients with diabetes, cardiovascular disease, etc., will benefit from having a beta blocker on board. One other thing that's not been mentioned is the rate pressure product and a drug that will not only lower blood pressure but also lower heart rate, I think is important as rate pressure product might be a better predictor as far as outcomes is concerned. It's a newer area of data, but I think it's something for us to think about. So I'll stop there with that agent and see if there are any questions for me on that. Otherwise, I'll move on to the other class of drugs.

Committee: Now, you are representing Forest...
Answer: Forest Laboratories, yes.

Okay, well I've also been asked to speak on the behalf of Tekturna (aliskiren) which is a direct renin inhibitor. Tekturna is the only agent in that class of drugs, and if we look at the history of blockade of the renin angiotensin aldosterone system, or RAAS system, we've wanted, really for a half century, to have an agent that would block this system at its initiation and we've finally got it almost two years ago when the drug was launched, but it took a long time to develop, and I think it's a very important drug for us to have for a number of reasons. For starters, when you look at hypertension, you're going to need multiple agents, and you need several drugs on board and drugs that are going to be well tolerated. Tekturna (aliskiren) is a very well tolerated agent. It compares in tolerability to the angiotensin receptor blockers. It's also a once-a-day agent and 24-hour ambulatory blood pressure studies show that it is effective throughout that 24-hour dosing interval, as far as sustained blood pressure reduction. As a nephrologist, we look at proteinuria, even though that is a surrogate marker, but we look at proteinuria to assess a patient's disease progression. That's probably the best predictor that we have for patients as far as progression of disease and who's going to wind up on dialysis, and what we're trying to do is slow progression of disease. We know that Tekturna by itself reduces proteinuria, but also in combination with an angiotensin receptor blocker, and it has been studied in combination with losartan, that there is an additional 20% reduction in proteinuria. So from a nephrologist's perspective, I think it's an excellent class of agents for us to have on board for hypertension, but also for the reduction in proteinuria. There is also emerging data on the cardiovascular side as far as reduction in BNP and pro-BNP levels that we look at. Are there any questions on that? Yes?

Committee: When you said it was well tolerated in your patient population, um, actually what we've seen with our Medicaid population is the drug being initiated, but then not continued. Have you had any patients that have not tolerated it well?
Answer: I've used the drug a lot over the last two years and I've had a very low failure rate, maybe two or three patients. I've seen it discontinued, mostly because of GI side effects, and that would probably be its main limitation.
Committee: I have a question. In our data for review, there were a couple of studies adding it in to an ACE or an ARB. Are you using it that way, or are you using it as a free standing agent?
Answer: Um, I use it both ways, but given that most people are already on a number of drugs by the time they come to me, most of my patients it is used, I use it as an add-on therapy to either an ACE or an ARB, in order to have dual blockade of the RAAS system.
Committee: And you are representing Novartis?
Answer: And representing Novartis.
Committee: Okay, thank you.

Ed Newcombe, MD
I'm Ed Newcombe, can you hear me? I'm Ed Newcombe, I'm in primary care internal medicine in Boise, and I've been asked to talk about Lipitor, and this is primarily through personal experience, because there are several studies out that suggest that Lipitor is quite beneficial in heading off strokes, heading off complications of myocardial disease, and just by personal experience, if I had one anti-lipid drug in my armormentarium, I would like that one to stay there. I understand it's on Medicaid as a primary drug right now, and I'm here just to vote to keep it there. This is largely because, in my experience, it's extremely well tolerated. I've had very few people who have not been able to tolerate it and I see a lot of diabetics with hypertriglyceridemia and it has been very effective in keeping the triglycerides down. I've seen a lot of people who have been switched by various insurance companies to other statins and their lipids have gone back up, triglycerides have significantly gone

up, and so I've put them back on the Lipitor and it stays down. There are several studies which you have all available already, so I won't go into a dissertation of all those, the TNT, the Scandinavian trial, the CARDS trial, I just would hope that you'd look at them.

Committee: And you're representing Pfizer?
Answer: They asked me to speak here, but they didn't pay me anything.

[laughter]

Will Watkins, MD
Good morning. I'm Will Watkins and I'm an urologist in Nampa, Idaho, where I work for the Idaho Urology Clinic and I'm here to speak on another tinkle topic, the enlarged prostate. I am here to hopefully convince you that you don't take Avodart or dutasteride off of the formulary. I do see Medicaid patients, probably less in my practice because I don't do pediatrics anymore. I've had the opportunity to use both drugs, Proscar and Avodart, over the years and I still use Proscar at the VA, because I see patients there once a week and I believe that dutasteride is better, faster and longer acting than Proscar. As you know, the Avodart is a 5-alpha reductase inhibitor and it works on both of the isoenzymes, both -1 and -2, and Proscar only works on -1. The studies have been done head to head, and it shows in the one study that I looked at about this, that the depression of dihydrotestosterone, the enzyme we're trying to suppress at 24 weeks was 6.62% with Proscar and 93% with Avodart. Another thing I think that is very important to explain the effectiveness of Avodart is that it has a very long half life. It's probably around five weeks and because of that, I find in my practice that when a patient reaches a study state at around 1-3 months, that I can reduce the dosage of Avodart. Usually, I tell them every other day, or if they have trouble remembering to do that, like I do, it would be three times per week. We know from studies that this is a very lasting drug, and it goes out over a period, it's been studied out as far as four years, and in fact at four years, the effectiveness seems to be increased. Now, by reducing the dosage over a period of time after they reach study state, there is a cost savings. Another cost saving is you may have heard that we use alpha blockers in patients with obstructive uropathy quite often, and I find that the patients who are on alpha blockers as well as the Avodart, I can stop the alpha blocker, often times at a month, maybe up to three months, but I can't stop the other drugs, so that way you can eliminate another drug. I'm here for my patients. I haven't contracted with Glaxo, who makes Avodart. They pay none of my expenses, they're not paying me any money, and in fact they don't give me pens or post-its or meals outside the office anymore. Can I answer any questions? Thank you.

Mandy Hosford
Good morning. I'm Dr. Mandy Hosford. I represent AstraZeneca Scientific Affairs in the Cardiovascular Division. I'll be speaking on two products this morning representing two different classes. It's Crestor for a pseudostatin, as well as Nexium on behalf of my GI colleagues. So since I have two products to speak about, I drank a lot of coffee this morning.

Committee: You didn't sign up twice, however.

Mandy Hosford, MD

I did not because in the past we had very limited time and I wanted to make sure that everyone had a chance, especially the physicians that took time away from their patients to speak. I stood before this committee last year to provide a label update for Crestor including slowing up the progression of atherosclerosis, and in response to the state's request for new and significant clinical information, I'm bringing to you not this year a label update, but rather a new clinical study that was reported for Crestor in November of last year. This is the JUPITER study. I'm not going to review the trial in great and gory detail for you all, because I expect that many of you are well aware of the study. I would just like to talk about kind of what it represents as decision makers for you on the P&T Committee. So briefly though, as I said, I won't review it, I'll just give some basics. This is the Crestor 20 mg versus placebo study in patients at low to intermediate risk for cardiovascular events not indicated to take a statin. Since I've said that, I need to make it clear that we as a company, and I do not condone or recommend the use of Crestor beyond what's indicated in the prescribing information, which includes indications to take a statin for hypertriglycemia. So just to briefly go over JUPITER again, Crestor 20 mg. This was a hard outcomes study versus placebo to look at whether or not the drug could reduce the risk of first heart attack, stroke be it fatal or non fatal, as well as hospitalization for unstable angina or need for arterial revascularization and the total mortality was also included in the primary end point. So what we did was essentially took about 17,000 patients, a median LDL 108 mg/dL, so these were essentially at goal, being low risk and really having one risk factor, which is their age. The other risk factor we looked at was high-sensitivity C-reactive protein >2 mg/L on two separate occasions, so this isn't just the acute upper respiratory infection, but rather chronically elevated marker of inflammation. These patients, over a median of about 2.8 years took Crestor 20 mg or placebo and we saw in the Crestor group in March of last year when we looked at all the data as, well, an independent data monitoring board looked at the data, they recognized a substantial reduction in events in those patients on active treatment versus placebo warranting a premature closure and stopping of the trial. So this represented, as we punched all the data, a relative risk reduction of about 44% at the primary end point, so this is a 54% reduction of heart attack, and as Dr. Newcombe pointed out, preventing stroke is of primary importance, and we saw a 48% relative risk reduction in stroke in these patients, as well as 47% reduction in the need for arterial revascularization or entering the hospital for a case of unstable angina. Total mortality was reduced by 20%. This was also statistically significant, and this was the first time in a primary prevention study; as you will recall these patients were not indicated to take a statin, that we saw a total mortality reduction in patients on treatment. The median LDL that was achieved on treatment was 55 mg/dL, reinforcing again what Dr. Newcombe said, that all the Lipitor studies really brought the field to focus on how low LDL is very important, and there were always questions as to whether or not that is safe. We see that, not only is it safe in getting LDLs to <70, even in the low to intermediate risk group, but we see substantial cardiovascular event risk reduction. So what's the summary here? Besides just dumping a lot of data on you, the purpose of this P&T Committee, the relevance in the study for you all is not necessarily to look at expanded use of lipid-lowering agents across different populations. This is not a guidelines recommendation. Rather, we just wanted to bring the data to the P&T Committee so that you all could say "We recognize now that Crestor has outcomes data in low, intermediate and high-risk patients" based on the heart failure study that I brought to you last year, and that the safety profile is consistent with all the agents in the class. We know that the statins are a very well studied and, for the most part, a very well tolerated group of drugs, again as Dr. Newcombe indicated, and I expect that his patients tolerate the agents that he requests that they initiate because of his confidence in them, and I appreciate that you all take the time to consider Crestor in addition to the preferred drug list for Idaho State Medicaid. Yes?

Committee: Drop out rate in the study? Placebo versus Crestor?

Answer: It was actually very low. Forgive me for not remembering the actual numbers, but I think we had about 88% completion in both arms, so the compliance was incredible. Discontinuation was actually less than what we would expect, so less than 10%. We intended, we thought we would have a lot of people dropping out, because these people are not indicated to take a statin, and we thought over 3-5 years, they may start to feel like "Why am I doing this?". I mean, it was very philanthropic of them, but we were impressed with the general level of compliance across both active treatment as well as placebo, and those discontinuation rates were statistically different. Does that answer your question? Any further questions? I'm sure that Dr. Liles will be able to address that as well.

Committee: Now, are you done, or?
Answer: Well, I'll just take another fifteen seconds, if I can comment then on Nexium on behalf of my GI colleague, again simply to provide a label update.

So Nexium has been indicated for the treatment of GERD, gastroesophageal reflux disease, thanks for letting me practice pronouncing that, in patients 12-17, and in February of 2008, those patients age 1 to 11 also received the indication for use of Nexium to prevent, or rather, to remediate GERD when lifestyle does not work; the smaller meals, more frequent, lifestyle changes. So I just really wanted to provide the Nexium indication update and I'd be happy to answer any questions on that if they exist. Yes?

Committee: Is there any indication for use of more than 40 mg of Nexium per day?
Answer: Um, at this point in time, there is not. I will actually briefly defer to my colleagues that work with the GI side more. That would not be considered an on label indication. Thank you again.

Roy Palmer, MD

Good morning, my name's Dr. Roy Palmer. I'm a Medical Director with Pfizer, and I'd just like to say a few words about atorvastatin or Lipitor. You know, you've had Lipitor on the PDL for the last several years, and I'd just like to reinforce some of the data that I think supports that decision. We've now completed over 400 different clinical trials with Lipitor and some of those have been lipid trials which have shown what it does to LDL and triglycerides, we've shown what it does with imaging studies to actually measure atherosclerosis and demonstrate progressions of atherosclerosis, and we've looked at inflammatory biomarkers, so if CLP is what you're interested in, we've shown dose related reductions in CLP up to 57%. But what we really put most of our effort and most of our weight on, is long-term outcome studies. We've studied both primary and secondary prevention, acute coronary syndrome patients, patients with diabetes, patients with hypertension, and pretty much any commonly found patient population who's going to receive a statin, in the clinic, has been studied in one of our long-term, 3-6-year studies. In fact, the ATP guideline changed the white paper which they published almost four years ago now, but the low goals were largely driven by data using atorvastatin. So we really believe we've led the field, we've studied just about anything you could imagine, in terms of patients who are going to receive this drug. Not only does that tell us a lot about the efficacy of the drug, but also a tremendous amount about safety. So when you do 3-6-year studies, there's no gaps in the safety. You're going to see exactly what it's like, especially in a broad patient population as we have done, and what we've seen is that it's very well tolerated, we don't see a dose response in safety, in fact at the 80 mg dose, we see equivalent safety to the 10 mg dose, and that's from studying over 14,000 different patients in, as I said, 3-6-year long-term studies. So that's really my summary to you. We've a tremendous amount of outcomes and safety data, and I hope that will be important in your decision making, and I'd like to ask you to keep Lipitor on the PDL for the patients of Idaho Medicaid. Thank you. Yes?

Committee: Is there any place overseas that Lipitor is available over-the-counter?
Answer: Uh, no, not over-the-counter anywhere, no. The only statin I know over-the-counter in the world is in England, they have a low dose Zocor (simvastatin).

Jennifer Brzana
Hello, my name is Jennifer Brzana, a Regional Medical Scientist with GlaxoSmithKline, speaking on behalf of Avodart, a 5-alpha reductase inhibitor, indicated for the treatment of BPH symptoms in men with an enlarged prostate. It's well established that prostate growth is driven by the entity in dihydrotestosterone or DHT. Testosterone is converted to DHT by the mechanism of two isoforms of the enzyme 5-alpha-reductase, both isoforms are found in the prostate, type-II is the predominant one, however it's type-I that plays a role in BPH and may become more important in prostate cancer. The therapy for enlarged prostate includes alpha-blockers, which improve symptoms, and the 5ARIs, which improve symptoms and consequently shrink the prostate by decreasing DHT. They also reduce the risk of long-term outcomes such as acute urinary retention and prostate-related surgeries. Three pieces of data I'd like to quickly review: Actually the first one was reviewed by Dr. Watkins showing greater DHT suppression with dutasteride versus finasteride, so I won't belabor that point. The second was published in the American Journal of Managed Care. ICA investigated the real-world experience with dutasteride and finasteride on the incidence of acute urinary retention and BPH-related surgeries in those with an enlarged prostate. The study utilized data from the Pharmatrics database and was collected over six years. Authors found that when compared to finasteride, Avodart patients were actually 49% less likely to have acute urinary retention and 41% less likely to have BPH-related surgeries, the latter was a statistically significant complaint. The third piece of data are the two-year results from the CombAT trial. This was published in the Journal of Urology. The CombAT study is four-year study, looking at combination therapy, alpha blocker and dutasteride versus each mono therapy alone, in controlling symptoms of BPH at two years and long-term outcome of surgery in acute

urinary retention at four years. The two-year results which have only been published to date show that the alpha blocker resulted in rapid symptom improvement, no surprise, but by month-15, both Avodart and tamsulosin had similar reductions in the symptoms of BPH, by month-21, Avodart was actually superior to the alpha blocker in controlling symptoms of BPH. Now looking at combination, it was superior to both monotherapy arms in month-3 versus Avodart and month-9 versus the alpha blocker. Avodart treats the cause of BPH and not just the symptoms. Therefore, it's an important option in the treatment of BPH to reduce not just symptoms, but long-term outcomes such as acute urinary retention and surgery. Based on its clinical findings, we recommend that Avodart be retained on the Idaho State PDL.

David Nilson
Good morning. My name is David Nilson, I'm a Regional Medical Scientist with GlaxoSmithKline. I wish to talk to you about Arixtra or fondaparinux, an injectable anticoagulant. It's a small-molecule synthetic, non-heparinoid, selective Xa inhibitor which binds to factor-III and potentiates more than 300 times its effect on factor Xa. Neutralization of factor Xa interrupts the blood coagulation cascade and thus inhibits thrombin formation and thrombus development. Fondaparinux does not inactivate thrombin and has no known effect on platelet function. At the recommended dose, fondaparinux does not affect fibrinolytic activity or bleeding time. It does not bind significantly to other plasma proteins, including platelet factor-IV or red blood cells, therefore does not cause heparin-induced thrombocytopenia. Fondaparinux reaches its peak concentration in 2-3 hours and is excreted unchanged in the urine. In the recent Chest guidelines in 2008, there's very favorable recommendations from Chest for fondaparinux. In all of the clinical trials, head to head with enoxaparin, they show a better efficacy and similar bleed rates, so the reasons to use fondaparinux or Arixtra is that it's always dosed once a day, it's synthetic, a non-heparin compound not derived from any animal sources, it's a specific factor Xa inhibitor, rapid onset of action, it does not inactivate thrombin, it's well tolerated with low rates of bleeding in all the clinical trials, outpatient treatment option for DVT and PE when initiated in the hospital. In the meta-analysis, Arixtra significantly reduced the risk of DVT/PE by about 55% compared with enoxaparin following orthopedic surgeries, it does not bind to factor-IV, therefore it doesn't cause HIT, and it's very easy to dose, especially for obese patients over 100 kg. There's one dose, 10 mg, for all patients, so it doesn't require the patient to calibrate and to maybe use a second syringe. Thank you.

Committee: We still have eleven speakers, so we'll try to get through as many as we can.

Pam Sardo
Thank you for the opportunity to come before you today to speak briefly about two products, TriCor and Simcor, on behalf of appropriate patients in Idaho. I'll try to give a little bit of time back to the Committee. Starting with TriCor, it is indicated as adjunctive therapy to diet to improve the parameters of total cholesterol, LDL, apolioprotein, HDL and triglycerides. With the nanocrystal technology, it can be administered without regard to food, unlike some of the other products that are on the market that do recommend taking with meals. In two studies of TriCor 145 mg daily, when the triglycerides were between 350 and 499, the triglycerides were improved by 46% and the HDL was improved by 19%. When the triglycerides were even higher, from 500-1500 mg/dyslipidemia, the TriCor, 145 mg resulted in an improvement of 54% of the triglycerides and also up to 22% in the HDL. So TriCor does have contraindications listed in the prescribing literature, and these do include hepatic or severe renal dysfunction in pre-existing gallbladder disease. So in conclusion, I wanted to thank you for the opportunity to suggest TriCor for the patients in need in Idaho. I'll answer any questions you have about TriCor. If not, I'll move on to Simcor. The health care community does recognize that hyperlipidemia is absolutely a medical problem and that the request and interest in reducing cardiovascular disease is important in many

populations, including diabetics and women. So with that in mind, it's well known that statins can reduce LDL by as much as 30-40%, however in spite of that LDL lowering, a residual cardiovascular disease risk does remain. With that in mind, the ATP III guidelines do recommend certainly lowering LDL as a primary target of therapy, but also they recognize non-HDL as a secondary target of therapy. So Simcor is a combination of the simvastatin and niacin extended-release, used as an adjunct to diet to help improve the parameters of LDL, non-HDL, total cholesterol, apoB, triglycerides, and to improve HDL in patients when the mono therapy does not allow those patients to get to goal. So Simcor does provide a choice of a combination therapy to assist with both compliance and convenience if it's necessary in appropriate patients. The SEACOAST study that was published in the American Journal of Cardiology in 2008 did show that the Simcor had a significant improvement in the non-HDL parameter beyond simvastatin 20 mg, and in the SEACOAST study, flushing did occur, but only resulted in discontinuation in 6% of those patient population. Also, Simcor does have contraindications also in the prescribing literature, and these do include active liver disease, active peptic ulcer disease and arterial bleeding. With that in mind, I would like to say in conclusion, thank you for your consideration of Simcor for the patients of Idaho as well. I'd be happy to answer any questions you might have regarding Simcor combination therapy.

Committee: Um, I didn't catch who you were representing?
Answer: I am so sorry. My brain was on how to create time. My name is Pam Sardo, I'm a Government Regional Clinical Executive, PharmD, with Abbott Laboratories. Any questions regarding Simcor or TriCor? Thank you.

Aaron Huwe
Good morning, Aaron Huwe, Senior Medical Scientist with Gilead Sciences. It's a pleasure to be here this morning and I do want to thank the Committee for their time. I'm pleased to provide a brief clinical update for Letairis or ambrisentan, which is the most recent therapeutic advance in the management of pulmonary arterial hypertension, which if you don't already know, is a rapidly progressive illness which afflicts about 80,000 Americans. Since ambrisentan offers major clinical advances over the five currently available treatments for PAH, the FDA granted a priority review and approved Letairis on June 15, 2007. Ambrisentan is an endothelin-A selective antagonist for the treatment of PAH in patients that are exhibiting WHO functional class-II or -III symptoms and this is in terms of improving exercise capacity or delaying the time of clinical worsening. It has been shown through many of the registrational studies that class-II and -III patients actually comprise about 70% of all PAH patients. The indication for Letairis is based on the results of two prospective comparative pivotal trials in ARIES-1 and ARIES-2. During these studies, 393 patients were randomized to receive one of three doses of ambrisentan, 2.5 mg, 5 mg or 10 mg, and these doses were then compared to placebo over the course of twelve weeks. For the primary end point, the six-minute walk distance, patients receiving ambrisentan had not only early and sustained, but also dose proportional benefit in the placebo adjusted mean increase from baseline to week-12 in the order of 31-59 meters. In addition, patients who received ambrisentan had a statistically significant delay in the time to clinical worsening, representing a 71% risk reduction, and just for your edification, clinical worsening has been defined as the first occurrence of one of six events: death, hospitalization for PAH, medications, lung transplant, atrial septostomy, and also study withdrawal due to early escape for advancing therapy. At the end of one year, 95% of patients survived compared to 16% that has been exhibited in some of the historical controls, particularly the NAH registry cohort from 1981-1987. Of the 295 patients who received ambrisentan for one year, 94% of these patients were still maintained on mono therapy and, as a side note, most recently at the Chest 2008 conference, the two-year data for Letairis was presented. Overall the Letairis product labeling includes two ERA box warnings: for potential for liver injury and also requiring monthly monitoring tests for LFT's in pregnancy. Because of the risks of liver injury and birth defects, Letairis is only available through a special restricted distribution access program called the LEAP,

Letairis Education and Access Program, and it's because of that, that only prescribers and pharmacies that are registered with this program may prescribe or distribute Letairis. Letairis received a potential liver injury box warning, despite a low incidence of LFT elevations, about 28% at twelve weeks, and the favorable results of an FDA-approved protocol known as ambrisentan-222, which demonstrated that 34 patients that had previously had LFT elevations on other ERA-type therapy, could successfully be treated with Letairis. Letairis is also pregnancy category X, and may cause fetal harm if taken during pregnancy. It's actually because of this fact that pregnancy must be excluded prior to the start of treatment and also prevented during treatment using two reliable forms of contraception. The incidence of treatment discontinuations due to adverse events other than those related to pulmonary hypertension during the clinical trials were similar between both the ambrisentan treatment group as well as placebo. The most common side effects in patients receiving ambrisentan included fluid retention and overall the current guidelines for PAH actually do not speak to Letairis and this is because of the data cutoff, we are anticipating a new update to the Chest Physician Guidelines in 2009 just to kind of keep you all aware of that, and I'd like to open up for any questions if possible. I'd like to thank you for your time. Thank you.

An Pham

Good morning. My name is Dr. An Pham. I'm a Cardiovascular Medical Science Liaison with Schering Plough Global Medical Affairs. I would like to thank the P&T Committee for the opportunity to provide public comment on the clinical benefit of Vytorin and Zetia and one important treatment options available to address hypercholesterolemia in the type 2 diabetic community, or a patient which is CHD equivalent. As you know, treating high-risk patients, including type 2 diabetics or CHD equivalent to prevent major cardiovascular events by reducing LDL cholesterol to a level below 70 is now recommended as an important therapeutic goal. In fact, the national guideline in the FDA reaffirmed that position, that lower is better when it comes to LDL cholesterol levels, based upon the most recently available clinical trials data and the totality of evidence from several decades of research. More importantly, cholesterol comes from multiple sources, including the diet that we consume and bile acid reabsorption in the liver. Zetia has a unique mechanism of action that blocks the absorption of cholesterol in the intestine, including cholesterol from both dietary and biliary sources. Zetia can be used as a mono therapy in patients who cannot tolerate statins. Adding on Zetia to a generic simvastatin first option or any statin offers treatment flexibility and plays an important treatment strategy in helping high-risk patients in Idaho to achieve incremental reduction in LDL cholesterol or to reach a level that is appropriate based on their risk factors. Alternatively, Vytorin in a single tablet offers superior lipid-lowering efficacy over Lipitor and Crestor from a starting dose of 10/20 mg through the synergy of ezetimibe and simvastatin. In summary, cardiovascular disease is a silent disease and quantitation drug adherence is critically important. Patients will likely adhere to a medication that is simple to take, well tolerated, and efficiently getting to goal at the starting of therapy. Vytorin offers that superior lipid-lowering efficacy from a starting dose of 10/20 mg, whereas Zetia offers treatment flexibility as an add-on therapy to a statin in helping high risk patients to reach their cholesterol goals. Zetia can also be used in statin-intolerant patients. I would like to thank you for the opportunity to provide these comments and your consideration. I would respectfully ask the P&T Committee to recommend Vytorin and Zetia to be added on to the Idaho State Medicaid Preferred Drug List. Now I would like to take any questions that you have. Thank you.

Leigh Platte

Good morning, my name is Leigh Platte and I'm the Scientific Liaison for Astellas and I'm here today to talk about VESIcare, solifenacin. The goal of therapy in these patients is to keep the patient dry and comfortable, with a minimum of side effects. In our registration trials, 51% of the patients were dry, and at the 5 mg dose, there was less than 11% rate of dry mouth. In the long-term trials, 81% of patients were still on the drug at the end of one calendar year and 61% of the patients were dry. In the STAR trial, solifenacin 5 mg and 10 mg versus Detrol LA 4 mg, 49% of

the patients on tolterodine were dry and 59% of the patients on the solifenacin. The secondary end points favored solifenacin in decreasing episodes of urgency, urge incontinence, and decreased pad usage, and also the patient's perception of their own bladder condition. We did two trials looking at urgency as a primary end point, and we chose urgency because the International Continence Society stated that urgency was the driving symptom of the overactive bladder complex. In patient focus groups, patients told us that urgency was the most bothersome symptoms for them, that fear of having a wetting accident in public. We also did warning time. A warning time was measured by a stopwatch. The patient's were told to start it when they felt that strong desire to void and to stop when they actually voided. The difference was 32 seconds. There was 32 seconds more time to try to find a bathroom. So in conclusion, in every clinical trial, at least half the patient's were dry, there was reasonable side effect profile, and they had some additional time to try to find a bathroom. Thank you very much. Are there any questions? Thank you, I appreciate your attention. So the first trial was called VENUS. Solifenacin was significantly superior to placebo in reducing episodes of urgency and urge incontinence with increasing warning time. Warning time is defined as that time from that compelling desire to void until you actually void. That was measured by a stopwatch. Patients had about an extra 32 seconds to hopefully find a bathroom or at least get out of public view. So hopefully that translates to some patient improvement. The secondary trial which looked at urgency as a primary end point was the SUNRISE trial, which was a European trial of 16 weeks in over 500 patients by an active drug. That not only looked at urgency, but also the severity of urgency. In that trial solifenacin was statistically superior in reducing episodes of severe urgency with or without incontinence, and the severity of all urgency. The most recent trial was VERSUS, which is focused on patients who continue to experience some residual urgency symptoms, despite at least four weeks of treatment with Detrol LA, and again there was a decrease in urgency and solafenacin had statistically significant improvement in urgency and other diary-documented symptoms of overactive bladder. So in summary, in every study we have looked at, there has been at least a 50% decrease in dry rates with these patients, and there has been significant improvement in quality of life and in decreased urgency episodes. Thank you very much. Are there any questions?

Jon Beaty

Good morning everybody. It's nice to see so many faces. I'm Jon Beaty. I'm with the Medical Affairs office for Boehinger Ingelheim Pharmaceuticals. I'm going to direct comments to your ARB review. Telmisartan requires and also the BHP agent reveiw some short comments about Flomax. Micardis is first. Also telmisartan, is indicated for the treatment of hypertension in monotherapy and in combination with other agents. The HCT formulation of telmisartan is not indicated for initial therapy. The antihypertensive efficacy of telmisartan has been studied in several specific hypertensive patient populations, which include those with essential hypertension, in the African American populations; type 2 and obese, overweight diabetes mellitus populations, and chronic kidney disease. The telmisartan label contains a box warning against the use of telmisartan in the second and third trimesters of pregnancy. In placebo-control trials involving patients treated from 12 mg to 160 mg of telmisartan for up to twelve weeks, an overall incidence of adverse effects was comparable to placebo, and the incidence of adverse events was not dose related and did not correlate in gender, the age or race. The safety and efficacy in pediatric patients hasn't been established for Micardis.

For Flomax, the approved indication is for the treatment of signs and symptoms of benign prostatic hyperplasia. It is not indicated for the treatment of hypertension. It's dosed once daily and does not require titration. Studies have demonstrated a rapid onset of action. An open labeled, multi-center, randomized, parallel designed study assessed the early onset of symptom improvement offered by Flomax 0.4 mg or terazosin with titration of 5 mg with patients with moderate to severe BPH symptoms. There was a statistically significant difference between Flomax and terazosin 1 mg in the change in total AUA symptom score based on into day-5, which was maintained over the entire study period.

Also studies have demonstrated long-term efficacy for Flomax. A six-year trial was completed, with Flomax representing the longest clinical trial data that's available for any alpha blocker. The study demonstrated sustained improvement in symptoms and flow rates, supporting durability in Flomax. As with other alpha blockers, there is potential risk for syncope and patients beginning treatment should be warned of this. The incidence of clinically significant hypertension and cardiovascular events recorded during trials with Flomax were low, and were not different from placebo. Intraoperative Floppy Iris Syndrome has been observed during cataract surgery in some patients treated with the alpha blockers. The benefit of stopping alpha-1 blocker therapy prior to cataract surgery has not been established. The most common side effects with Flomax were dizziness, abnormal ejaculation, and rhinitis. That completes my statements that I have to present to you and I'd be happy to answer any questions. Thank you.

Committee: I think we have time for one more speaker. Long Nguyen. For those of you have signed up and didn't get to speak, I apologize. We are limited to 60 minutes for public testimony. If you send in a written transcript of what you were going to say, I (Bob Faller) will get it to all of the P&T members.

Long Nguyen, PharmD

Good morning. My name's Long Nguyen, PharmD, representing GlaxoSmithKline, and I wanted to talk to you about Lovaza and its benefit to patients. Lovaza is FDA-approved to use as a mono therapy in patients who have very high triglycerides ≥500 mg/dyslipidemia at a dose of 4 gm per day. Lovaza is highly purified Omega-3 fatty acids, containing 84% of EPA/DHA per 1 gm capsule. In comparison to dietary supplementation, fish oil products sold in stores; a 1 gm capsule contained about 30% of EPA/DHA. Therefore, it takes roughly 10-12 capsules of the dietary supplement fish oil to get an equivalent amount of EPA/DHA in 4 gm capsules of Lovaza. Since Lovaza is derived from fish, it's a natural product, and it has been used in Europe for more than ten years. Because Lovaza is not metabolized by the liver cytochrome P450 or cleared by the kidney, there is no drug-drug interactions expected with Lovaza. The only notable side effects reported by patients taking Lovaza were taste perversion and eructation. To further demonstrate and confirm that Lovaza is safe and effective, additional safety information was added to the PI based on the results of the COMBOS study. The COMBOS study is a randomized, double-blind, placebo study that looked at 254 patients who were already on simvastatin for their lipids, who were added 4 gm of Lovaza in addition, shows that there are no drug interactions both in pharmacokinetic and pharmacodynamic parameters and show an additional 30% reduction in triglycerides, a 9% reduction in non-HDL, and 3.4% increase in HDL in addition to statins. Compared to other triglyceride-lowering drugs available, such as Gemfibrozil and fenofibrates which are contraindicated to use with statins because of the high risk of developing rhabdomyolysis and myopathy. Furthermore, fibrates are contraindicated in patients with hepatic and renal dysfunction according to the package insert. No such contraindications or warnings with Lovaza, other than a potential increase incidents of bruising in patients taking Lovaza concomitant with anticoagulants. The most frequently asked questions to me by health care providers and patients is, "Since this is a natural product from fish, how much fish should I take to get an equivalent amount of EPA/DHA in Lovaza?" and to give you an idea, a multiple number of studies have indicated that to get an equivalent amount of EPA/DHA in fish to get a 1 gm capsule of Lovaza, you have to take in 23 lbs of cod per day, 12 oz of tuna, or 20 lbs of catfish, and up to and from 5-8 lbs of salmon per day. Based on the benefits, safety and efficacy of Lovaza compared to other lipotropic agents and the differences of Lovaza in dietary supplements available over-the-counter, I would request that the Committee consider Lovaza to be available to

patients who have triglycerides greater than 500 mg/dyslipidemia. With that, I would be happy to answer or address any questions that the Committee members may have.

Question: You said "taste perversion and what was the second?"
Answer: Eructations, which is a kind of like nausea, vomiting, and those tend to be very consistent with a high amount of fatty acid. We see based on our clinical experience and clinical experience from physicians using Lovaza in patients who are on dietary supplements, it is dose related, so the patients who take 10-12 capsules of fatty acid tend to have higher side effect of taste perversion and eructation compared to Lovaza. Any other questions I can address? Thank you very much.

Dina Noble
I'm Dina Noble and I'm from Allergan Medical Affairs, and thank you for your consideration of hearing my spiel on Sanctura XR, which is known as trospium. To be very concise with your time, the overactive bladder drugs as a category is recognized to be equally efficacious. What I would ask for your consideration as a committee member is to think about the advantage of this drug from a different quarternary amine profile. As a pharmacist, what this would confer is an advantage of less CNS penetration and thus a potential for CNS adverse effects. The other main consideration that I think of is that, from a metabolism viewpoint, it doesn't go through the P450 isoenzyme system, so patients who are on a lot of medications that go through the hepatic system, you can potentially avoid this. You do have to consider the renal elimination. 60% of it is renally excreted through the endothelium, so what you do think of that is the drug interaction profile for renal tubular secreted drugs, such as [illegible], procanimide and metformin. So metformin to me would be a big issue from the diabetes perceptive in the clinical trials. Patients who were also on the metformin, they didn't see any adverse reactions, but I would be thinking of lactic acidosis, but that was not noted as an AE. If you look in your overview provided by Provider Synergies and you look at the adverse effect profiles, you will see for the most part that there are minimal adverse effects associated with this drug; dry mouth being the most common intolerance for this. So basically, I really do appreciate your consideration of Sanctura, coming here from Mississippi. Should I practice my drawl a little bit more? Thank you.

Committee: Sue, did you want to speak at this time?

Sue Heineman
Um, if you don't mind, and for all of you who know me, I live here and I'm a pharmacist, and I always try to make my comments as being applicable to you. I'm always the last one that comes up because you guys see me as a breath of fresh air or that you're relieved that we're almost done. But for Detrol LA, tolterodine long acting, there's not a lot of new data, but I do want to just remind you of what has happened to the providers in the state. When Detrol was preferred, tolterodine ER was preferred in 2005 and 2006, there were 55% of the patients who were on it. In 2007, it was removed and it was the only agent that was put on the non-preferred and there were no safety changes, there were no efficacy changes, and I think it's probably had the most breadth of data. Now it's back on and currently if you guys take a look at your utilization, 50% is generic, and when you look at the branded agents, tolterodine is about 10% and a couple of others have about that 10% share, so it's being used appropriately and I would just ask that you consider the impact on the providers if you start asking again to say "All right, you have to switch patients off tolterodine ER", so that's all, and I do appreciate what you're doing and the opportunity to speak.